REMARKS

The limitations of claims 83 and 84 have been inserted into claim 72 in the alternative. Claim 72 has also been amended to specify 20P1F12/TMPRSS2 as either the nucleotide sequence SEQ. ID. No.: 1 or the cDNA in ATCC deposit 207097; therefore 20P1F12/TMPRSS2 protein is the protein encoded by these nucleotide sequences. These identifiers are as set forth in the application as originally filed. No new matter has been added and entry of the amendment is respectfully requested.

Applicants have demonstrated that the nucleotide sequence set forth in SEQ. ID. No.: 1 is overexpressed in prostate cancer and various other cancer cell lines (see Figure 7). The only overexpression detected in normal tissue is in prostate, an organ that is entirely non-essential and disposable. Accordingly, as correctly pointed out by the Office, this selective expression identifies the protein as a suitable target for inhibiting cancer cell growth, viability or survivability. The following response is to the specific objections and rejections set forth by the Office.

Objections to the Specification

As a separate document herewith, amendment has been made to eliminate any possible embedded hyperlink; applicants believe the amendment is sufficient; if the Examiner believes that further amendment is required, a telephone call to the undersigned is respectfully requested.

A revised sequence listing in compliance with 37 C.F.R. §§ 1.821-1.825 is also submitted herewith.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 72-82 were rejected as being incomplete; claims 83 and 84 were not included in this rejection. The limitations of claims 83 and 84 have been inserted into claim 72 in the

alternative. All other claims depend from claim 72. Therefore, it is believed that the amendment is completely responsive to this rejection which therefore may be withdrawn.

The Rejections Under 35 U.S.C. § 112, First Paragraph of Claims 72-82.

These claims were rejected on the basis that "modulating the status" of cancer cells does not find support in the specification. While applicants disagree that this phrasing is beyond the scope of the specification, the limitations of claims 83 and 84, which were not included in this basis for rejection have been imported into claim 72, from which all other claims depend. Accordingly, this basis for rejection may also be withdrawn.

The Rejection of Claims 72-84 Under 35 U.S.C. § 112, First Paragraph - "20P1F12/TMPRSS2-Related" Proteins:

This basis for rejection has also been addressed by amendment. The Office objects that the specification teaches only the expression product of the 20P1F12/TMPRSS2 gene. The amendment to the claims addresses this basis for rejection by specifying that the protein is the product of SEQ. ID. No.: 1 or the ATCC deposit which contains it. Accordingly, this basis for rejection may also be withdrawn.

The Rejection of Claims 72-84 Under 35 U.S.C. § 112, First Paragraph - Unpredictability

Much of the substance of this rejection is based on an asserted unpredictability of cancer treatment. Respectfully, applicants point out that the method claimed need not be itself a treatment method. The ability to effect the inhibition of growth, viability and/or survivability of cancer cells using an antibody directed to 20P1F12/TMPRSS2 is diagnostic of the expression of that protein in the cells. Since the protein contains a serine protease domain, for example, (see page 7, lines 36, *et seq.*) serine protease inhibitors as potential treatments are suggested. Thus, the claimed method provides valuable information regarding treatment modalities.

The Office interprets the claims as also including instances where antibodies or fragments thereof that are specific for the target protein are administered to humans to treat cancer. The Office asserts that the expectation of success of such treatments is so low that the disclosure in the specification is insufficient to show possession of the invention. Respectfully, it appears that the documents assembled by the Office in support of its position instead support patentability of these claims. (In addition, the method is useful even if no treatment is accomplished as set forth in the previous discussion.)

First, the Office cites U.S. patent 5,770,195 which claims a method of inhibiting the growth of tumor cells by treating with an antibody to the HER-2 receptor. This treatment, as the Office is aware, is currently being administered to actual people in clinics. The claims in the '195 patent issued without such clinical proof of efficacy. In addition, applicants are unable to find in the specification of the '195 patent, any discussion of the occurrence of the HER-2 receptor in normal tissue, one way or the other; it is known in the art that HER-2 is actually expressed on cardiac tissue, but this is considered an acceptable risk.

The Weiner article cited by the Office states that there are a number of successful tumor treatments using antibodies or fragments, citing, in Table 5, on page 49, a number of such treatments with "promising results." The comments made by the Office that "antigenic heterogenicity" and "insufficient target specificity" are obstacles to successful antibody therapy is noted, but its relevance to the present disclosure is not seen. No antigen heterogenicity is contemplated - the claim now specifies a particular gene product. Further, the only normal tissue which shows expression levels that might be considered troublesome is the prostate itself. This is seen in Figure 6 which shows only marginal amounts of expression in kidney, pancreas and even less in lung, as compared to normal prostate. Figure 7, noted by the Office in the context of

this rejection shows results only for tumor cell lines. Thus, normal tissue expression is significant only in the prostate. Should the prostate be destroyed in the process of treating the malignancy, this would not be fatal or even particularly deleterious to the subject. Accordingly, these disadvantages are not associated with the present claims. It is also unclear why relative scarcity of tumor-specific antigens is relevant when the tumor-specific antigen of interest has already been identified in the present application.

As to the putative lack of specific demonstration of growth inhibition of tumor cells in the application, as the Office is aware, this is not required by law. As demonstrated by the Weiner document, the utility described by the application is perfectly credible.

The Office goes on to state that treatment of cancer is unpredictable. First, the Office cites Gura, *Science* (1997) which discusses the difficulty of extrapolating from preliminary *in vitro* or *in vivo* protocols, and in particular from animal models to humans. Of course, the correlation between success in these models and in the clinic is not perfect; however, such success, for example, in animal models is hardly irrelevant or meaningless. If it were, then it would not be the case, as it is the case, that everybody uses them. The underlying statement that model systems are "not predictive" was not regarded as defeating of patentability in the holding in *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995) which explicitly points out that it is almost always the case that further experimentation and development will be needed in order to make the transition between a patentable discovery and clinical approval. As the Court pointed out, its precedent clearly holds that actual clinical experience is unnecessary to provide sufficient basis for patentability.

With regard to Bellone and Gaiger, these documents are not relevant as they pertain to eliciting an immune response using the antigen itself; the claims are directed to direct treatment of the antigen using antibodies or fragments thereof.

Thus, taken in total, the art cited by the Office supports applicants' position. Bellone and Gaiger are irrelevant to the subject matter claimed; the proposition for which Gura stands has been held by the Federal Circuit to be irrelevant to patentability. The Weiner document shows that antibody therapy of cancer has a track record of success. The undeniable fact that not all patients are cured or even helped by such therapies is true of any presently employed therapeutic method. This does not mean that the method is not enabled or not useful.

For the reasons stated above, it is respectfully submitted that the present specification clearly shows the compliance of the specification with 35 U.S.C. § 112, first paragraph, in support of the patentability of claims 72-82.

CONCLUSION

The claims have been amended to incorporate the limitations of claims 83 and 84 into claim 72, thus obviating the rejection under 35 U.S.C. § 112, paragraph 2, and one of the three bases for rejection under § 112, paragraph 1. Further, claim 72 has been amended to clarify that the protein to which the antibodies are bound is the gene product of the nucleotide SEQ. ID. No.: 1 or of the corresponding ATCC deposit. This obviates the second basis for rejection under § 112, paragraph 1. Respectfully, the third basis under § 112, paragraph 1, has been shown to be in error since (a) there is no requirement that the application demonstrate actual reduction to practice so long as the description teaches how to make and use the invention and (b) no document has been cited which supports the position of the Office to doubt the teachings of the specification. The objection that the antigen occurs on normal prostate does not defeat

credibility in view of the fact that the prostate is a non-essential organ. Accordingly, it is believed that claims 72-82 are now in a position for allowance and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 511582000800.

Respectfully submitted,

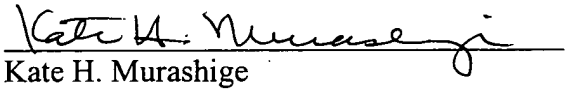
Dated: February 24, 2003 By: 

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EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

72. (Amended) A method for [modulating the status] inhibiting the growth, viability and/or survivability of cancer cells that express the nucleotide sequence SEQ. ID. No.: 1 or the cDNA in ATCC deposit 207097 (20P1F12/TMPRSS2), the method comprising:

administering to the cancer cells an antibody or fragment thereof that specifically binds to a 20P1F12/TMPRSS2[-related] protein, [whereby the status of a cell that expresses 20P1F12/TMPRSS2 is modulated] thereby inhibiting the growth, viability and/or survivability of said cancer cells.

74. (Amended) The method of claim 72, wherein said antibody or fragment is a recombinant protein comprising the antigen-binding region of an antibody that specifically binds to [a] 20P1F12/TMPRSS2[-related] protein.